

Urinary Tract Infections

Magdalena Sobieszczyk, MD MPH
Division of Infectious Diseases
Columbia University

Clinical Scenario #1

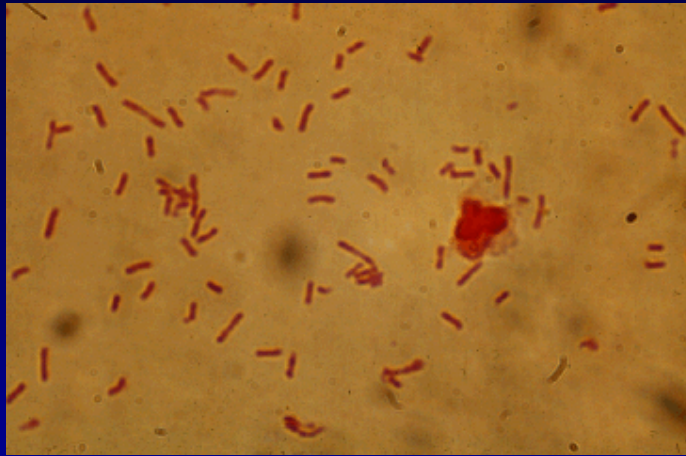
- 23 y.o woman presents to her doctor complaining of 1 day of increased urinary frequency, dysuria and sensation of incomplete voiding
- She is otherwise healthy, takes no medications, and is sexually active, using spermicide-coated condoms for contraception. She says she does not have fever, chills, vaginal discharge, or flank pain
- Sexually active with one partner, no hx/o sexually transmitted diseases

Clinical Scenario #1

- She looks a little uncomfortable but is afebrile, with a normal blood pressure
- Her abdominal exam is notable for mild suprapubic tenderness, no RUQ tenderness, no costovertebral tenderness
- Pelvic exam is deferred

Clinical Scenario #1 : Labs

- Urinalysis: pyuria (WBC too numerous to count), RBC and bacteria present
- Urine dipstick: positive leukocyte esterase and nitrite
- Urine culture: not done
- Patient receives 3 days of TMP/SMX for UTI



Gram stain of urine shows numerous Gram-negative rods.
E.coli grew from this urine specimen

Urinary Tract Infections

- Definitions
- Clinical Symptoms and Diagnosis
- Microbiology and Epidemiology
- Pathogenesis
 - Host Factors
 - Bacterial Factors
- Clinical Scenario
- Treatment and Prevention

UTI: Definitions

- **Lower UTI:** cystitis, urethritis, prostatitis
- **Upper UTI:** pyelonephritis, intra-renal abscess, perinephric abscess (usually late complications of pyelonephritis)
- **Uncomplicated UTI** – Infection in a structurally and neurologically normal urinary tract. Simple cystitis of short (1-5 day) duration
- **Complicated UTI** – Infection in a urinary tract with functional or structural abnormalities (ex. indwelling catheters and renal calculi). Cystitis of long duration or hemorrhagic cystitis.

UTI: Clinical Symptoms and Presentation

- Cystitis in the adult:
 - Dysuria, urinary urgency and frequency, bladder fullness/discomfort
 - Hemorrhagic cystitis (bloody urine) reported in as many as 10% of cases of UTI in otherwise healthy women
- Pyelonephritis (upper UTI) in the adult:
 - Fever, sweating
 - Nausea, vomiting, flank pain, dysuria
 - Signs and symptoms of dehydration, hypotension
- A history of vaginal discharge suggests that vaginitis, cervicitis, or pelvic inflammatory disease is responsible for symptoms of dysuria (pelvic examination)
 - Important additional information includes a history of prior sexually transmitted disease (STD) and multiple current sexual partners.
- UTI in children:
 - < 2 years - enuresis, fever, poor weight gain
 - > 3 years - dysuria, lower abdominal pain

Diagnosis of UTI

- U/A microscopic examination
 - WBC, RBC
 - Presence of bacteria
- Urine dipstick test: rapid screening test
 - leukocyte esterase test
 - Nitrate → nitrite test (+ in only 25%)
- Indications for urine culture
 - Pyelonephritis
 - Children, pregnant women
 - Patients with structural abnormalities of the urinary tract

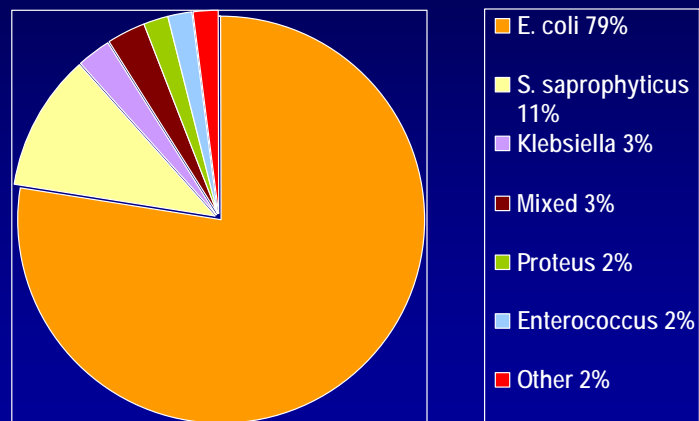
Indications for Evaluating the Urinary Tract

- Children
 - ultrasound, IVP, CT scan
- Bacteremic pyelonephritis not responding to therapy
 - ultrasound, IVP, CT scan
- Nephrolithiasis or Neurogenic Bladder
 - Ultrasound, CT, or IVP with post-voiding films
- Men with 1st or 2nd infection
 - Careful prostate examination
 - Ultrasound or IVP with post-voiding films

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Etiology of Uncomplicated UTI in Sexually Active Women



Microbial Species Most Often Associated with Specific Types of UTI's

<i>Organism</i>	<i>Acute uncomplicated cystitis</i>	<i>Acute uncomplicated pyelonephritis</i>	<i>Complicated UTI</i>	<i>Catheter-associated UTI</i>
<i>E.coli</i>	79%	89%	32%	24%
<i>S. saprophyticus</i>	11%	0%	1%	0%
<i>P. mirabilis</i>	2%	4%	4%	6%
<i>Klebsiella</i> spp.	3%	4%	5%	8%
<i>Enterococcus</i> spp.	2%	0%	22%	7%
<i>Ps. aeruginosa</i>	0%	0%	20%	9%
Mixed	3%	5%	10%	11%
Other*	0%	2%	5%	10%
<i>Candida</i> spp.	0%	0%	1%	28%
<i>S. epidermidis</i>	0%	0%	15%	8%

**Serratia, Providencia, Enterobacter, Acinetobacter, Citrobacter*

UTI: Epidemiology and Risk Factors by Age Group

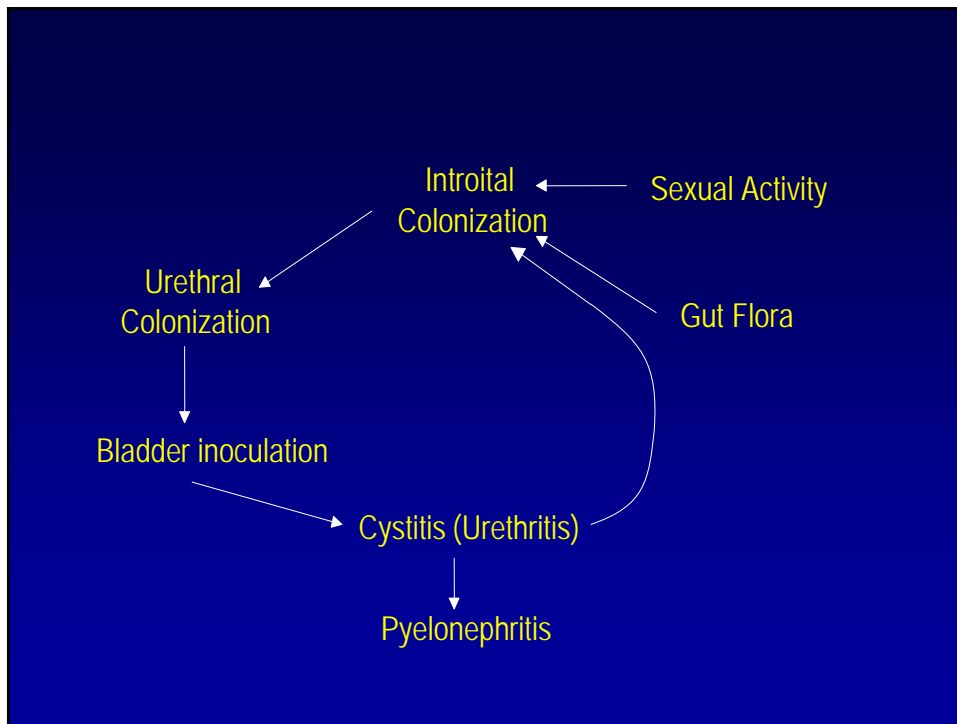
Age in years	Females (% Prevalence)	Males (% Prevalence)
< 1	Anatomic/functional abnormalities (1%)	Anatomic/functional abnormalities (1%)
1-5	Congenital abnormalities, Vesicoureteral reflux (4.5%)	Congenital abnormalities, uncircumcised penis (0.5%)
6-15	Vesicoureteral reflux (4.5%)	Vesicoureteral reflux (0.5%)
16-35	Sexual intercourse, spermicide use, previous UTI (20%)	Anatomic, insertive anal intercourse (0.5%)
36-65	Gynecologic surgery, bladder prolapse (35%)	Prostate hypertrophy, obstruction, catheterization (20%)
>65	Estrogen deficiency and loss of lactobacilli (40%)	All of the above; urinary catheters (35%)

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Pathogenesis of UTI

- Hematogenous Route
- Ascending Route
 - Colonization of the vaginal introitus
 - Colonization of the urethra
 - Entry into the bladder
 - Infection



UTI in Women: Factors Predisposing to Infection

- Short urethra
- Sexual intercourse & lack of post coital voiding
- Diaphragm, spermicide use
- Estrogen deficiency
- P₁ blood group - upper UTI

Host Factors Predisposing to Infection

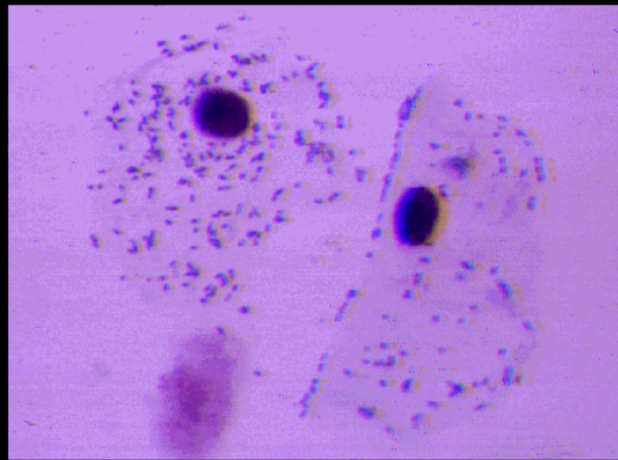
- Extra-renal obstruction
 - Posterior urethral valves
 - Urethral strictures
- Renal calculi
- Incomplete bladder emptying
- Neurogenic bladder
- Immunocompromised individuals (e.g. DM, transplant recipients)

Bacterial Virulence Factors-I

- Enhanced adherence to receptors on uroepithelial cells
 - **Type 1 fimbriae:** mediate binding to uroplakins, mannosylated glycoproteins on the surface of bladder uroepithelial cells
 - **P fimbriae:** bind to galactose disaccharide on the surface of uroepithelial cells and to P blood group antigen (D-galactose-D-galactose residue) on RBCs
 - 97% of women with **recurrent pyelo** are P1 blood group (+)
 - Higher prevalence of P-fimbriated *E.coli* in cystitis-causing strains than in strains from asymptomatic persons (60% vs. 10%)
- Phase variation:
 - Type 1 fimbriae increase susceptibility to phagocytosis, P-fimbriae block phagocytosis
 - In strains that cause upper-tract infections: Type 1 down-regulated, Type P upregulated (PAP gene expression triggered by temperature, [glucose], concentration of certain amino acids)



Electron microscopic view of an *E.coli* showing the fimbriae (pili) bristling from the bacterial cell wall



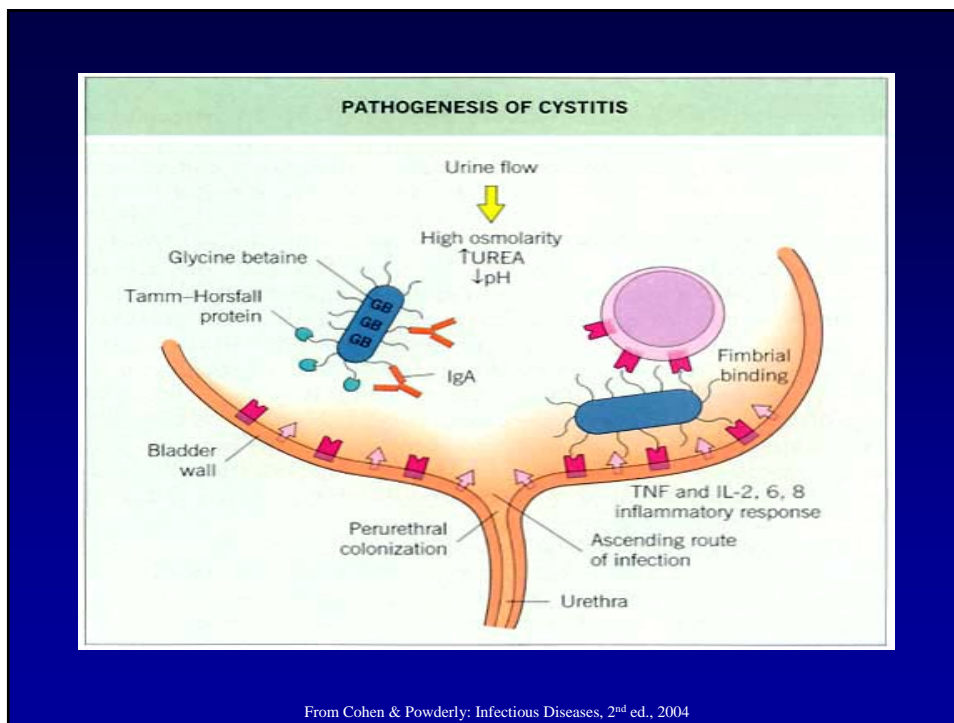
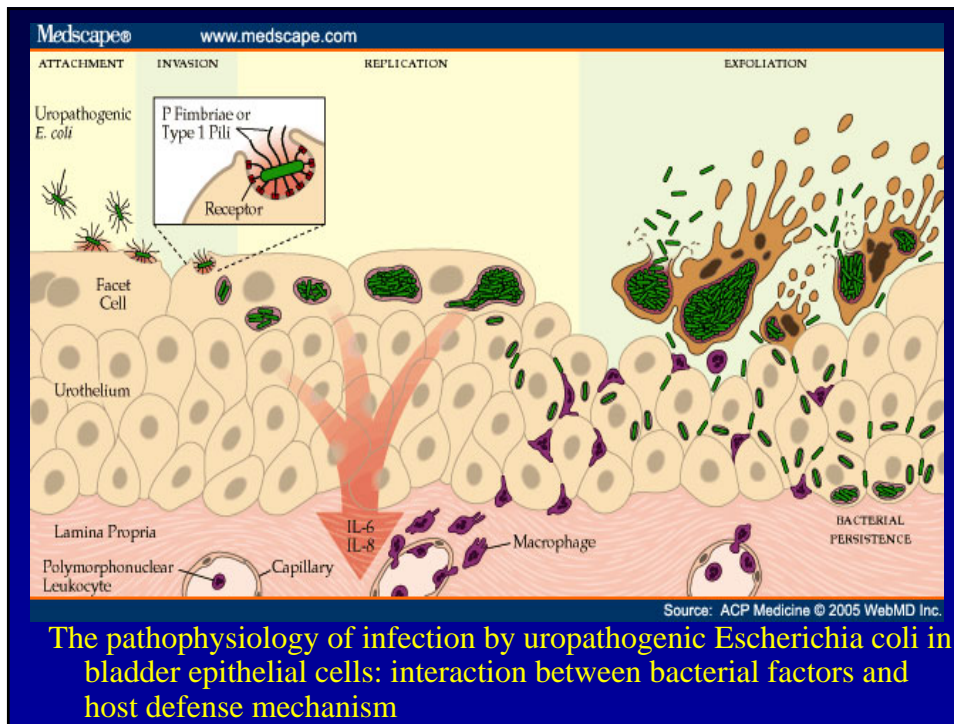
Increased adhesion with uropathogenic *E. coli* Adherence of uropathogenic *Escherichia coli* onto uroepithelial cells. Courtesy of Agnès Labigne, MD, Institut Pasteur, Paris.

Bacterial Virulence Factors-II

- Flagella- enhanced motility
- Production of hemolysin → induces pore formation in cell membrane → cell lysis (nutrient release)
- Production of aerobactin (a siderophore) → iron acquisition in the iron-poor environment of the urinary tract

Antibacterial Host Defenses

- Urine flow and micturition
- Urine osmolality and pH
- Inflammatory response (PMNs, cytokines)
- Inhibitors of bacterial adherence
 - Bladder mucopolysaccharides
 - Secretory immunoglobulin A



Clinical Scenario #2

- 43 y.o woman with DM presents to the ER complaining of chills, nausea and low back pain for the past 2 days. Earlier in the week she developed increased urinary frequency and dysuria.
- Recognizing the symptoms of UTI she took two days of TMP/SMX but was unable to finish treatment because of nausea and vomiting
- Past medical history is notable for frequent UTIs treated with TMP/SMX and a history of Diabetes Mellitus
- No hx/o STDs, no vaginal discharge

Clinical Scenario #2

- She looks unwell and appears uncomfortable
- She is febrile to 101.2, tachycardic to 100 with a BP 100/60
- On exam her mucous membranes are dry; there is suprapubic tenderness, and severe right flank and right costovertebral tenderness
- Urinalysis, Urine microscopic examination and urine culture are performed: pyuria, hematuria, bacteriuria
- Blood cultures are drawn
- Patient is admitted to the hospital for IV antibiotics and pain management

Clinical Scenario #2

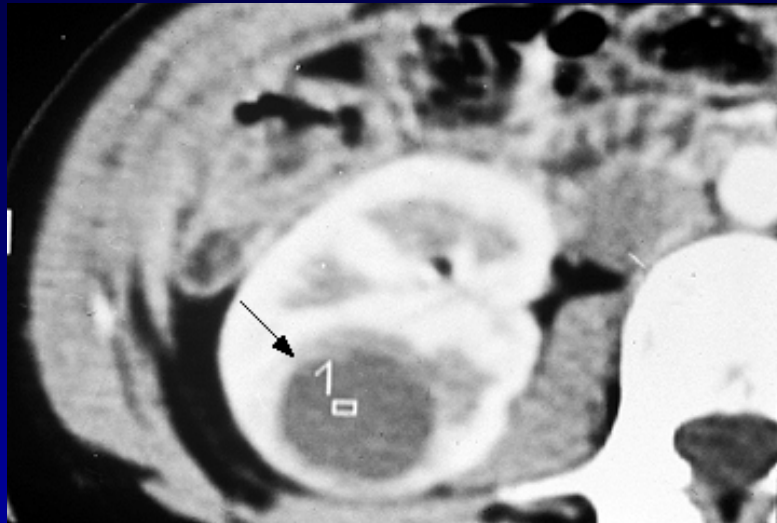
- The next day, urine and blood cultures show Gram-negative rods
- After 72 hours of hydration and intravenous antibiotics your patient is still febrile and repeat urine examination is still notable for pyuria and bacteriuria
- You are concerned about
 - urinary obstruction
 - intrarenal/perinephric abscess
 - infection with resistant organism

Clinical Scenario #2

- Microbiology lab informs you that the the pathogen is an *E.coli* sensitive to fluoroquinolones, resistant to TMP/SMX
- Renal CT is notable for a large renal abscess
- Diagnosis: pyelonephritis complicated by a renal abscess in a diabetic patient



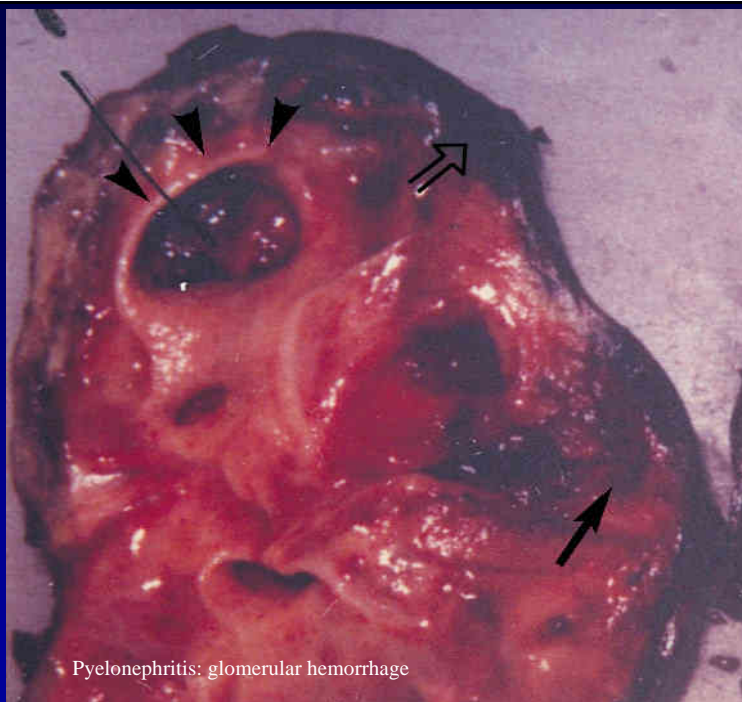
Renal abscess on ultrasonography Ultrasonic examination of the kidney showing an abscess cavity (arrow). The internal echoes within the lesion can also be seen with a malignancy but not with a simple cyst. Courtesy of Alain Meyrier, MD.



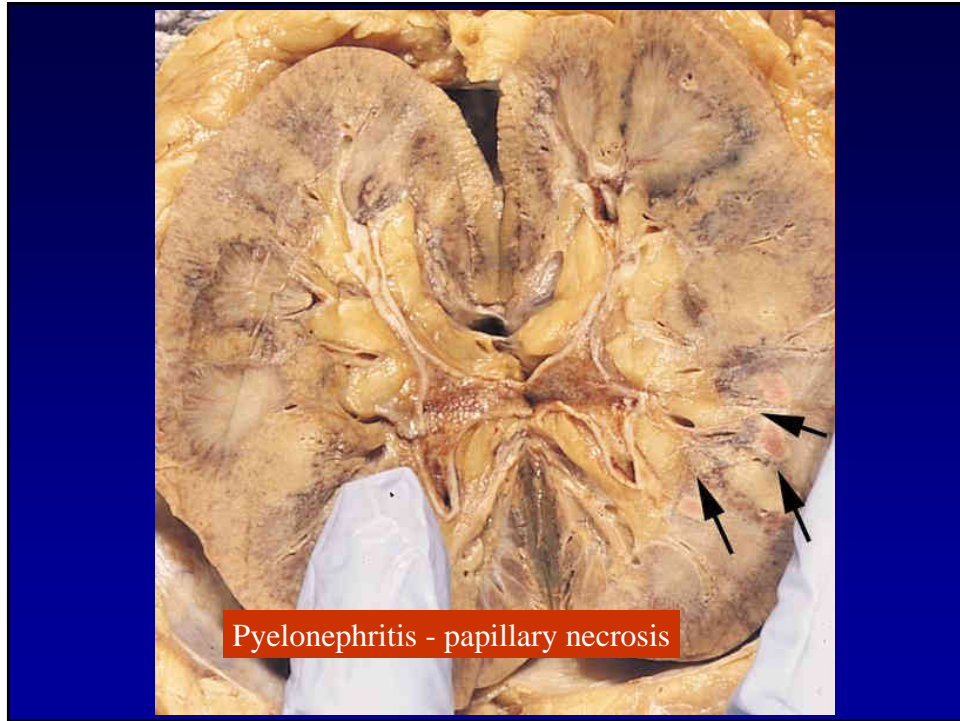
Renal abscesses on CT scan CT scan showing a large renal abscess with internal echoes in the right kidney (arrow). Courtesy of Alain Meyrier, MD.

UTI: Upper Tract Disease

- Symptoms suggestive of upper tract disease (pyelonephritis):
 - Fever (usually greater than 101° F.),
 - Nausea, vomiting, and
 - Pain in the costovertebral areas
 - Urinary frequency, urgency and dysuria
 - Renal abscess: patients with urinary tract abnormalities, diabetic patients
- Evaluation: urine culture, +/- blood cultures,
 - Imaging if no improvement
- Microbiology: *E.coli*, and *Citrobacter*, *Pseudomonas aeruginosa*, *Enterococci*, *Staphylococcus* spp.
- Initial therapy: intravenous antibiotics for 10-14 days (perinephric abscess treat longer, +/- drainage)



Pyelonephritis: glomerular hemorrhage



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Treatment: General Principles

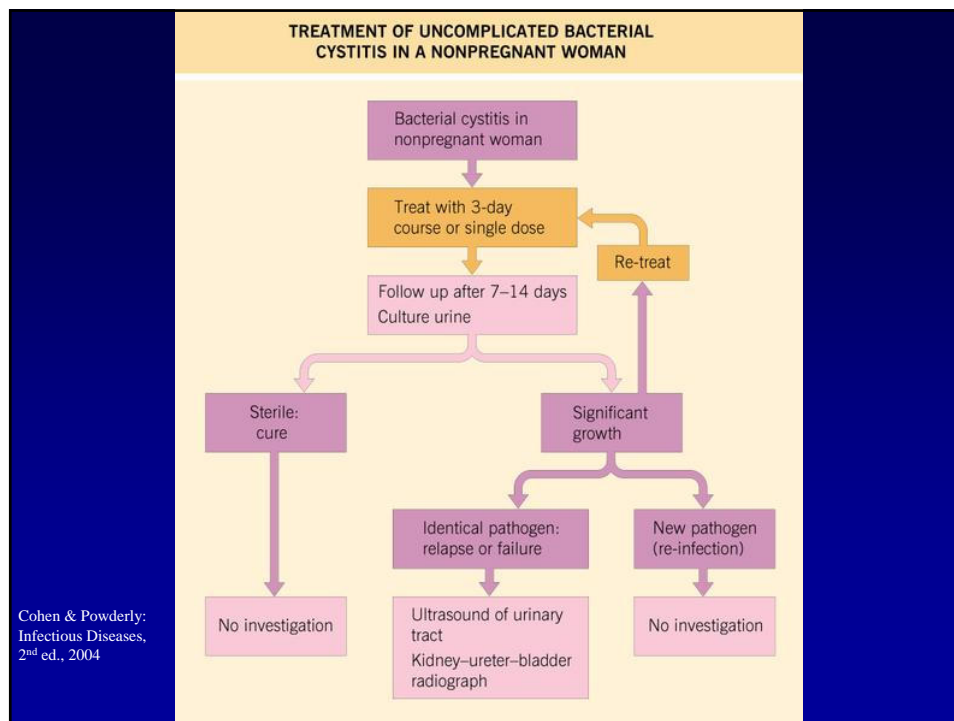
- Quantitative cultures may be unnecessary before treatment of typical cases of acute uncomplicated cystitis.
- Culture urine in patients with upper UTI, complicated UTI, or with treatment failure.
- Susceptibility testing is necessary in all recurrent or complicated infections, perhaps not for uncomplicated cases.
- Identify or correct factors predisposing to infection
 - Obstruction, calculi
 - Diabetic patients who are at risk for recurrent infections, pyelonephritis and perinephric abscesses

Treatment: General Principles

- Recurrent infections common in young women (20% by 6 months).
 - Majority are exogenous infections rather than failure to cure initial infection
- Duration of therapy depends on the site and duration of the infection.

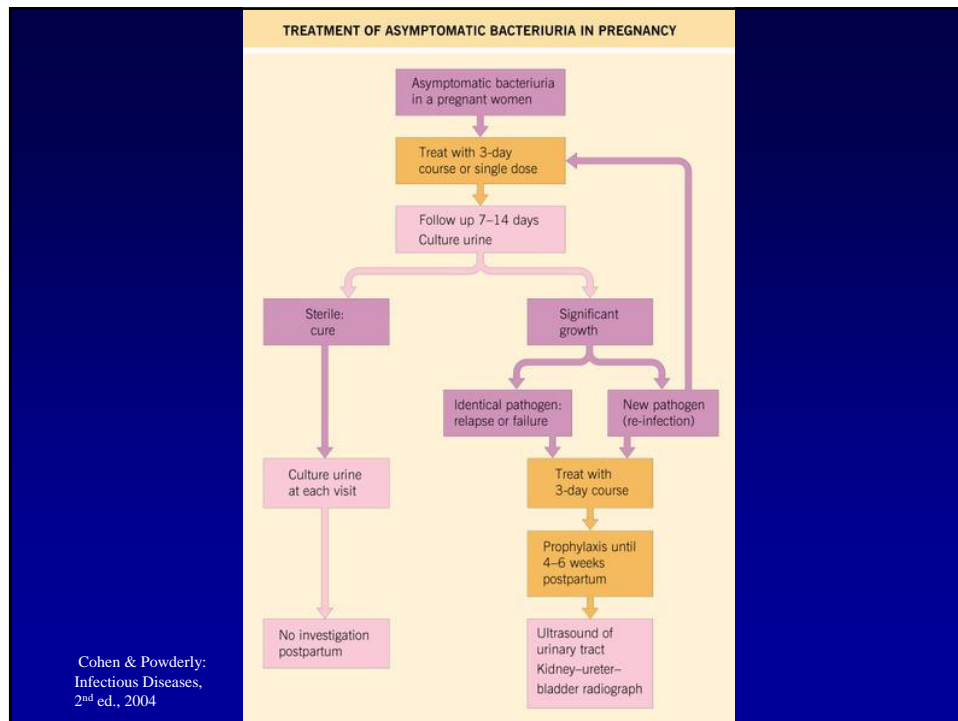
Empiric Antimicrobials

- Choice of antimicrobial agents
 - Primary excretion routes through the urinary tract
 - Achieve high concentration in urine and vaginal secretions
 - Inhibit *E.coli*, the primary pathogen in cystitis
- Short course (3-day) therapy for uncomplicated infections
- Longer duration (10-14 days) for complicated infection (e.g. pyelonephritis)
- Oral vs. intravenous agents (TMP/SMX, Fluoroquinolones)



Treatment of Asymptomatic Bacteriuria

- Pregnant women
- Patients with neurological or structural abnormality of the urinary tract
- Patients undergoing urologic surgery

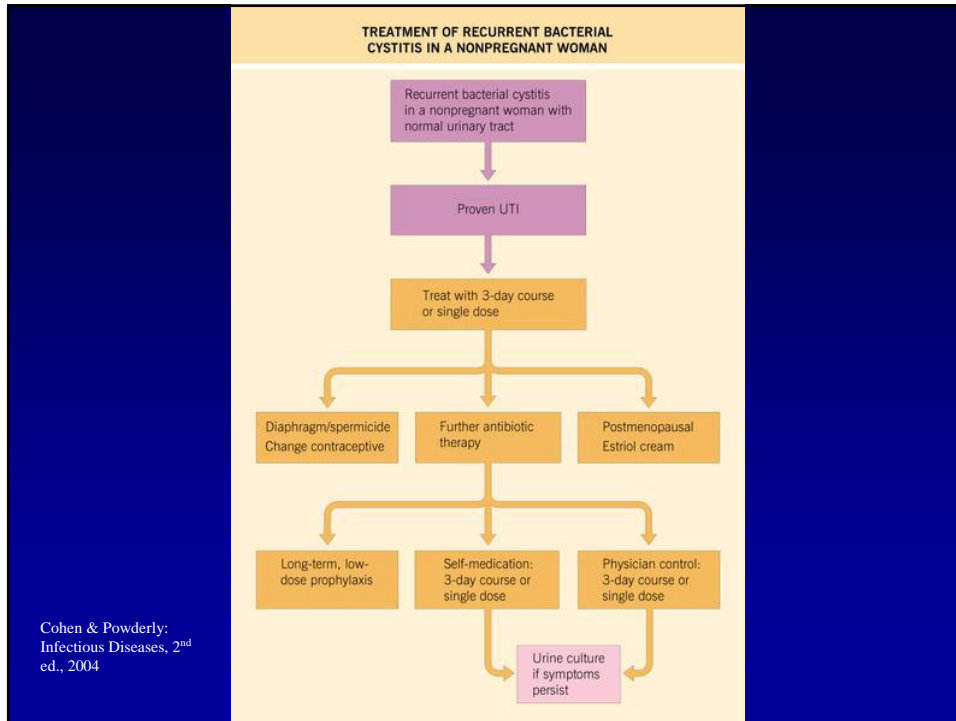


Recurrent UTI

- Risk factors for recurrent uncomplicated UTI
 - P1 blood group positive; postmenopausal status; diabetes
 - Recent antimicrobial use
 - Behavioral risk factors (spermicide use, new partner, first UTI <15 y.o.)


Prevention Strategies

- Prevention Strategies
 - Alternative methods of contraception
 - Postcoital voiding and increased fluid intake
 - Cranberry juice (sexually active women with previous UTI)
 - Antibiotic prophylaxis
 - >2 symptomatic UTIs within six months or >3 over 12 months
 - Postcoital prophylaxis vs. continuous prophylaxis vs. self-treatment



Antimicrobial Resistance

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WIDESPREAD DISTRIBUTION OF URINARY TRACT INFECTIONS CAUSED BY A MULTIDRUG-RESISTANT *ESCHERICHIA COLI* CLONAL GROUP

AMEE R. MANGES, M.P.H., JAMES R. JOHNSON, M.D., BETSY FOXMAN, Ph.D., TIMOTHY T. O'BRYAN, KATHLEEN E. FULLERTON, M.P.H., AND LEE W. RILEY, M.D.

- Reports of increased resistance to TMP/SMX
- Regional variation
- Rates between 18-40%

Selected References

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